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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/479,252	01/07/2000	Avi J. Ashkenazi	P0978P3C1	2825

7590

11/19/2001

GENENTECH INC  
Attn Diane L Marschang  
1 DNA Way  
South San Francisco, CA 94080-4990

EXAMINER

BUNNER, BRIDGET E

ART UNIT

PAPER NUMBER

1647

DATE MAILED: 11/19/2001

9

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/479,252

Applicant(s)

ASHKENAZI ET AL.

Examiner

Bridget E. Bunner

Art Unit

1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 20 September 2001.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1,3-6,18,19,22 and 25 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,3-6,18,19,22 and 25 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 15.
- 4) ☐ Interview Summary (PTO-413) Paper No(s) \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

## DETAILED ACTION

### *Status of Application, Amendments and/or Claims*

The amendments of 07 January 2000 (Paper No. 2) and 20 September 2001 (Paper No. 7) have been entered in full. Claims 7-17, 20-21, 23-24, and 26 are cancelled.

### *Election/Restrictions*

Applicant's election of Group I, claims 1, 3-6, 18-19, 22, and 25 in Paper No. 7 (20 September 2001) is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 1, 3-6, 18-19, 22, and 25 are under consideration in the instant application.

### *Sequence Compliance*

1. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2).

**Specifically, the sequences disclosed in Figure 1B are not accompanied by the required reference to the relevant sequence identifiers. Additionally, the claims recite figure numbers rather than sequence identifiers.** This application fails to comply with the requirements of 37 CFR 1.821 through 1.825. Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825).

Appropriate correction is required.

### *Specification*

2. An updated status of the parent nonprovisional applications should be included in the first sentence of the specification. A statement reading "This is a continuation of U.S. Application

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No. 09/060,533, filed April 15, 1998, now abandoned, which is a continuation-in-part of U.S.

Application No. 09/007,886, filed January 15, 1998, now abandoned, which is a continuation-in-part of U.S. Application No. 780,496, filed January 8, 1997, Patent No. 6,046,048, which claims benefit of U.S. Application No. 60/009,755, filed January 9, 1996" should be entered.

Appropriate correction is required.

***Claim Rejections - 35 USC § 102***

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

4. Claims 1, 3-6, 18-19, 22, and 25 are rejected under 35 U.S.C. 102(a) as being anticipated by Wiley et al. (Immunity 3(6): 673-682, Dec. 1995).

Wiley et al. teach an isolated soluble protein, designated TNF-related apoptosis-inducing ligand (TRAIL) that is 100% identical to the Apo-2 ligand polypeptide of the instant application comprising amino acids 91-281 of SEQ ID NO: 1 (see sequence alignment attached to this Office Action as Appendix A; see pg 675, col 1 and amino acids 91-281 of Wiley et al.; see also Figure 1A and amino acids 91-281 of SEQ ID NO: 1 of the instant application). The TRAIL protein identified by Wiley et al. that corresponds to amino acids 91-281 of SEQ ID NO: 1 of the instant application comprises an N-terminal methionine residue (see sequence alignment attached to this Office Action as Appendix A; see amino acids 91-281 of Wiley et al.). Additionally,

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Wiley et al. disclose that TRAIL induces apoptosis in many different types of cells, including mammalian cancer cells (pg 675-676; pg 678, col 1-2; Table 1). Wiley et al. treat the cells with conditioned supernatant from cells transfected with the soluble TRAIL construct, which is a composition (pg 680, ¶ 2).

5. Claims 1, 3-6, 18-19, 22, and 25 are rejected under 35 U.S.C. 102(e) as being anticipated by Wiley et al. (U.S. patent 5,763,223).

Wiley et al. teach an isolated soluble protein, designated TNF-related apoptosis-inducing ligand (TRAIL) that is 100% identical to the Apo-2 ligand polypeptide of the instant application comprising amino acids 91-281 of SEQ ID NO: 1 (see sequence alignment attached to this Office Action as Appendix A; see col 28-29, example 7 and amino acids 91-281 of Wiley et al.; see also Figure 1A and amino acids 91-281 of SEQ ID NO: 1 of the instant application). The TRAIL protein identified by Wiley et al. that corresponds to amino acids 91-281 of SEQ ID NO: 1 of the instant application comprises an N-terminal methionine residue (see sequence alignment attached to this Office Action as Appendix A; see amino acids 91-281 of Wiley et al.).

Additionally, Wiley et al. disclose that TRAIL induces apoptosis in many different types of cells, including leukemia and lymphoma cells (col 26-27, example 5; col 29-30, example 8 ; Table 1).

Wiley et al. also teach that TRAIL has the ability to kill leukemia and lymphoma cells (col 30, example 9). Wiley et al. treat the cells with conditioned supernatant of CV1/EBNA cells transfected with the soluble TRAIL construct, which is a composition (col 28-29, example 7).

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***Conclusion***

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (703) 305-7148. The examiner can normally be reached on 8:00-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (703) 308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

BEB  
Art Unit 1647  
November 14, 2001



ELIZABETH KEMMERER  
PRIMARY EXAMINER

## ALIGNMENTS

RESULT 1  
TN10\_HUMAN STANDARD; PRT; 281 AA.  
ID TN10\_HUMAN STANDARD; PRT; 281 AA.  
AC P50591;  
DT 01-OCT-1996 (Rel. 34, last sequence update)  
DT 01-OCT-1996 (Rel. 34, last sequence update)  
DT 01-OCT-2000 (Rel. 40, last annotation update)  
DE TUMOR NECROSIS FACTOR LIGAND SUPERFAMILY MEMBER 10 (TNF-RELATED  
DE APOPTOSIS INDUCING LIGAND) (TRAIL PROTEIN) (APO-2 LIGAND) (APO-2L).  
GN TNFSF10 OR TRAIL OR APO2L.  
OS Homo sapiens (Human).  
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
OC Mammalia; Eutheria; Primates; Catarrhini; Hominoidea; Homo.  
OX NCBI\_TaxID=9606;  
RN [1]  
RA MEDLINE=66111955; PubMed=8777713;  
RA Wiley S.R., Schooley K., Smolak P.J., Din W.S., Huang C.-P.,  
RA Nicholl J.K., Sutherland G.R., Davis-Smith T., Rauch C., Smith C.A.,  
RA Goodwin R.G.;  
RT "Identification and characterization of a new member of the TNF  
RT family that induces apoptosis.";  
RL Immunity 3:673-682(1995).  
RN [2]  
RA SEQUENCE FROM N.A.  
RA TISSUE=Placenta;  
RA MEDLINE=96278649; PubMed=8663110;  
RA Pitti R.M., Masters S.A., Ruppert S., Donahue C.J., Moore A.,  
RA Ashkenazi A.;  
RT "Induction of apoptosis by Apo-2 ligand, a new member of the tumor  
RT necrosis factor cytokine family.";  
RL J. Biol. Chem. 271:12687-12690(1996).  
CC -1- FUNCTION: INDUCES APOPTOSIS.  
CC -1- SUBUNIT: HOMOTRIMER (POTENTIAL).  
CC -1- SUBCELLULAR LOCATION: TYPE II MEMBRANE PROTEIN (POTENTIAL).  
CC -1- TISSUE SPECIFICITY: WIDESPREAD; MOST PREDOMINANT IN SPLEEN, LUNG  
CC AND PROSTATE.  
CC -1- SIMILARITY: BELONGS TO THE TUMOR NECROSIS FACTOR FAMILY.  
CC -----  
CC This SWISS-PROT entry is copyright. It is produced through a collaboration  
CC between the Swiss Institute of Bioinformatics and the EMBL outstation -  
CC the European Bioinformatics Institute. There are no restrictions on its  
CC use by non-profit institutions as long as its content is in no way  
CC modified and this statement is not removed. Usage by and for commercial  
CC entities requires a license agreement (See <http://www.isb-sib.ch/announce/>  
CC or send an email to [license@isb-sib.ch](mailto:license@isb-sib.ch)).  
CC -----  
CC EMBL: U37518; AAC50332.1; -  
CC EMBL: U57059; AAB01233.1; -  
CC MIM: 603598; -  
CC InterPro: IPR000478; -  
CC Pfam: PF00229; TNF\_1; 1.  
CC PROSITE: PS00251; TNF\_1; 1.  
CC PROSITE: PS50049; TNF\_2; 1.  
CC Cytokine; Transmembrane; Signal-anchor; Apoptosis.  
FT DOMAIN 1  
FT 17 CYTOPLASMIC (POTENTIAL).

FT TRANSMEM 18 38 SIGNAL-ANCHOR (TYPE-II MEMBRANE PROTEIN).  
FT DOMAIN 39 281 EXTRACELLULAR (POTENTIAL).  
SQ SEQUENCE 281 AA; 32509 MW; DDAALF78DAAB2FED CRC64;

Query Match 100.0%; Score 996; DB 1; Length 281;  
Best Local Similarity 100.0%; Pred. No. 1, le-78;  
Matches 191; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 MLRTSEETISTVQEKQONISPLVERGQRYVAHITGRGNSNTLSSPNSKNEKALGRK 60  
DB 91 MLRTSEETISTVQEKQONISPLVERGQRYVAHITGRGNSNTLSSPNSKNEKALGRK 150  
QY 61 INSWESSRSGHSFLSNLHNGELVTHEKGFYIYSQTFERFOEIKENTKNDKQWQYI 120  
DB 151 INSWESSRSGHSFLSNLHNGELVTHEKGFYIYSQTFERFOEIKENTKNDKQWQYI 210  
QY 121 YKTSYDPDILLKMSARNSCWDKDAEYGLYSIYOGGIFELKENDRIYVSTNEHLIDMDH 180  
DB 211 YKTSYDPDILLKMSARNSCWDKDAEYGLYSIYOGGIFELKENDRIYVSTNEHLIDMDH 270  
QY 181 EASFGAFIVG 191  
DB 271 EASFGAFIVG 281

# Appendix B

## ALIGNMENTS

RESULT 1  
 US-08-670-354-2  
 ; Sequence 2, Application US/08670354  
 ; Patent No. 5763223  
 ; GENERAL INFORMATION:  
 ; APPLICANT: Steven R. Wiley and  
 ; APPLICANT: Raymond G. Goodwin.  
 ; TITLE OF INVENTION: Cytokine That Induces Apoptosis  
 ; NUMBER OF SEQUENCES: 9  
 ; CORRESPONDENCE ADDRESS:  
 ; ADDRESSEE: Kathryn A. Anderson, Immunex Corporation  
 ; STREET: 51 University Street  
 ; CITY: Seattle  
 ; STATE: WA  
 ; COUNTRY: USA  
 ; ZIP: 98101  
 ; COMPUTER READABLE FORM:  
 ; MEDIUM TYPE: Floppy disk-  
 ; COMPUTER: Apple Macintosh  
 ; OPERATING SYSTEM: Apple 7.5.2  
 ; SOFTWARE: Microsoft Word, Version 6.0.1  
 ; CURRENT APPLICATION DATA:  
 ; APPLICATION NUMBER: US/08/670,354  
 ; FILING DATE: 25-JUN-1996  
 ; CLASSIFICATION: 435  
 ; PRIORITY APPLICATION DATA:  
 ; APPLICATION NUMBER: US 08/496,632  
 ; FILING DATE: 29-JUN-1995  
 ; CLASSIFICATION: 435  
 ; PRIOR APPLICATION DATA:  
 ; APPLICATION NUMBER: US 08/548,368  
 ; FILING DATE: 01-NOV-1995  
 ; CLASSIFICATION: 435  
 ; ATTORNEY/AGENT INFORMATION:  
 ; NAME: Anderson, Kathryn A.  
 ; REGISTRATION NUMBER: 32,172  
 ; REFERENCE/DOCKET NUMBER: 2835-B  
 ; TELECOMMUNICATION INFORMATION:  
 ; TELEPHONE: (206) 587-0430  
 ; TELEFAX: (206) 233-0644  
 ; TELEX: 756622  
 ; INFORMATION FOR SEQ ID NO: 2:  
 ; SEQUENCE CHARACTERISTICS:  
 ; LENGTH: 281 amino acids  
 ; TYPE: amino acid  
 ; TOPOLOGY: linear  
 ; MOLECULE TYPE: protein  
 ; US-08-670-354-2

us-09-479-252-1

Query Match 100.0%; Score 996; DB 1; Length 281;  
 Best Local Similarity 100.0%; Pred. No. 3.8e-98;  
 Matches 191; Conservative 0; Mismatches 0; Indels 0; Gaps 0;  
 OY 1 MIIPTSEETISTVOEKOONISPLVREBGPORVAHAHTITGRGRSNTLSSPNKNEKALCRK 60  
 DB 91 MIIPTSEETISTVOEKOONISPLVREBGPORVAHAHTITGRGRSNTLSSPNKNEKALCRK 150  
 OY 61 INSWESSRSGHSEFLSNLRLNGELVYHEKGFYIYSQYFFRFOEIKENTNDKQVOYI 120  
 DB 151 INSWESSRSGHSEFLSNLRLNGELVYHEKGFYIYSQYFFRFOEIKENTNDKQVOYI 210  
 OY 121 YKITYSPDPIILMKARSNCWCKDAEYGLYSIYOGGIFELKENDRIEVSVTNEHLIDMDH 180  
 DB 211 YKITYSPDPIILMKARSNCWCKDAEYGLYSIYOGGIFELKENDRIEVSVTNEHLIDMDH 270  
 OY 181 EASFEGATLVG 191  
 DB 271 EASFEGATLVG 281